

31
34.

(New) A method of rendering a tissue or organ suitable for transplantation, comprising expressing a polypeptide according to claim 22 in endothelial cells in said tissue or organ, thereby down-regulating the expression of a cell adhesion molecule.

Rule
12631
Amended32
35.

(New) A method of transplantation, comprising transplanting biological tissue according to claim 31 from a donor animal into a recipient animal.

REMARKS

The claims are amended to correspond with the claims as they were amended during the International phase of the application, and to remove multiple dependency. No new matter is added.

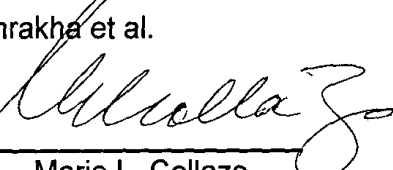
Replacement pages 24-25 are enclosed.

Entry of this amendment is respectfully requested.

Respectfully submitted,

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20. A biological tissue comprising endothelial cells which may be induced to generate a compound which down-regulates the expression of a cell adhesion molecule by the cells, the compound being either (a) a polynucleotide complementary in sequence to part of the gene or mRNA that encodes the cell adhesion molecule, (b) a polynucleotide comprising a ribozyme sequence that specifically targets a gene or mRNA that encodes the cell adhesion molecule, or (c) a peptide or polypeptide with specific binding affinity for the cell adhesion molecule.
21. A tissue according to claim 20, wherein said polypeptide (c) is a bispecific fusion protein.
22. A polypeptide comprising a binding region capable of binding to a cell adhesion molecule and a signalling region for subcellular targeting of the polypeptide such that is not transported to the cell surface.
23. A polypeptide according to claim 22, which comprises an antibody or antibody fragment.
24. A polypeptide according to claim 23, which comprises a single chain Fv fragment.
25. A polypeptide according to claim 22, wherein the signalling region for subcellular targeting of the polypeptide comprises a localisation signal for the endoplasmic reticulum.
26. A polypeptide according to claim 25, wherein the signalling region comprises the amino acid sequence KDEL at the C terminus of the polypeptide.

27. A polypeptide according to claim 22, wherein said binding region has affinity for any one of the adhesion molecules VCAM-1, ICAM-1, LFA-1, CD2, PECAM, CD31, IAP, CD47 or integrin $\alpha v \beta 3$.
28. A polynucleotide encoding a polypeptide according to claim 22.
29. A vector comprising a polynucleotide according to claim 28.
30. A cell comprising a polynucleotide according to claim 28 or a vector according to claim 29.
31. Biological tissue comprising a cell according to claim 30.
32. A non-human animal comprising biological tissue according to claim 31 and/or a cell according to claim 30.
33. An animal according to claim 32, wherein said animal is a transgenic pig or sheep.
34. A method of rendering a tissue or organ suitable for transplantation, comprising expressing a polypeptide according to claim 22 in endothelial cells in said tissue or organ, thereby down-regulating the expression of a cell adhesion molecule.
35. A method of transplantation, comprising transplanting biological tissue according to claim 31 from a donor animal into a recipient animal.